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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,187	07/30/2003	Jurgen Engel	103832-477-NP	9817

7590 02/12/2007

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,187	ENGEL ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or ~~(f)~~.

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **9/21/06**presents remarks and arguments to the office action mailed **3/24/06**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nickel et al., 6,093,704 and Nickel et al., 6,696,428 and Nossner et al. 6,172,050 (all references already of record) in view of Calabresi et al., Goodman & Gilman's, The Pharmacological Basis of Therapeutics, Ninth Edition.

Applicant argues that the Calabresi et al, only teach a list of known anti-tumor agents for treating cancer and does not teach the specific combination of the instantly claimed subject matter.

In response Applicant is only focusing on one reference Calabresi et al. However, the test for obviousness is not whether the features of a secondary reference

may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Whether or not Calbresi teaches the specific combination or not, it is supported by the Goodman and Gilman that cancer drugs give adage to treatment of cancers when combined with other antineoplastic agents. The Nickel et al. teach administering miltefosine to breast cancer rats. The drug is used to treat breast cancer and nothing unobvious is seen in combining the drug with another antineoplastic agent.

Applicant's arguments filed have been fully considered but they are not persuasive. The reasons are set forth above and the rejection is maintained as in the last office action of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

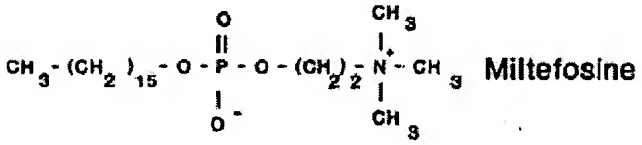
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-6 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilgard et al. cancer Chemother. Pharmcol. (1993) 32: 90-95 in view of Stekar et al. European J. of Cancer Vol. 31(3) pp 372-374, 1995 (from Applicant submitted ref.).

Hilgard et al. teach compound of formula I



Miltefosine

wherein n is 2, m is 0, R is $C_1 - C_{20}$ as in the instant claim 1 (see page 91, lft. col.) for the treatment of mammary carcinoma (see page 91 under Activity of miltefosine highlighted sec.) in combination with cisplatin (see page 93, highlighted sec.) as in claims 1-2, 5-6 and 9-12.

With regards to claim 2 R is $C_1 - C_{17}$ (see page 91, n is 2, X is O), wherein the alkylphosphocholine is in a carrier (see page 93, last line).

Stekar et al. teach the drug miltefosine is administered before or prior to the administration of cyclophophamide (see page 373, rt. col.) as in claims 4 and 12.

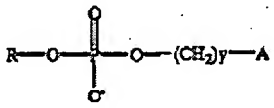
One of ordinary skill in the art would have been motivated to combine the above cited references and administered miltefosine prior to administering the antitumor substance cyclophosphamide because the reference teaches so.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

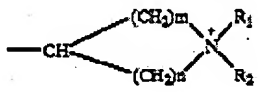
Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilgard et al. Cancer Chemother. Pharmcol. (1993) 32: 90-95 taken with Stekar et al. European J. of Cancer Vol. 31(3) pp 372-374, 1995 in view of Nössner et al. US 6,172,050.

Hilgard et al. and Stekar et al. are applied here as above.

Nössner et al. disclose alkylphosphocholine compounds and their use in pharmaceutical compositions for treating tumors, wherein the tumor is breast cancer (see col. 20, line 57). The compounds are represented by the following General



wherein A is the ring system



Formula (I): wherein the compound is Octadecyl-1,1-dimethylpiperidinio-4-yl phosphate (see col. 6, lines 45-50) as in the instant claims 3 and 4. Col. 19, lines 34-45 teaches that the above compound can be administered in a regimen and lines 48-54 teaches the different agent that the above compound formula can be combined with cisplatin, cyclophosphamide (see col. lines 50-51) in a

pharmaceutically effective amount (see col. 20, lines 42-44) in a carrier or excipient (see same col.).

Although the cited references did not directly teach the compounds are heterocyclic compounds, it is known fact to one of ordinary skill in the art that cyclophosphamide is a heterocyclic compound as in claims 7-8. Therefore the art teaches the compounds of the instant claims 7-8.

One of ordinary skill would have been motivated to combine the above cited prior art and make and use the claimed invention at the time it was made because the prior art teaches that the compounds of both formulae I and II have been used before the claimed invention was made to treat breast cancer. The motivation comes from the teachings of the prior art as already cited.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H. Marschel 2/4/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

SVG
1/30/07